

IN THE CLAIMS:

1. (Previously Presented) An aqueous dispersion of hydrogel nanoparticles, comprising:
interpenetrating polymer network (“IPN”) nanoparticles, wherein each IPN nanoparticle comprises a first polymer network interpenetrating a second polymer network; and
an aqueous medium;
wherein, the first polymer comprises poly(N-isopropylacrylamide) or hydroxypropylcellulose, and the second polymer comprises poly(acrylic acid);
wherein, the IPN nanoparticles are substantially free of a core-shell polymer configuration; and the aqueous dispersion of hydrogel nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon; and
wherein, the aqueous dispersion exhibits a change in particle size of less than 30 nm when the aqueous dispersion is heated from below a volume phase transition temperature to above a volume phase transition temperature at a concentration of 2.88×10^{-5} g/ml.
2. (Original) The aqueous dispersion of hydrogel nanoparticles of claim 1, further comprising a biologically active material.
3. (Previously Presented) The aqueous dispersion of hydrogel nanoparticles of claim 2 wherein the biologically active material is: a drug, a pro-drug, a protein, a nucleic acid, or a mixture thereof.
4. (Original) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the stimulus comprises a change in temperature.
5. (Previously Presented) The aqueous dispersion of hydrogel nanoparticles of claim 4, wherein the temperature change above a gelation temperature (“Tg”) induces a volume phase transition of the IPN nanoparticles, resulting in an inverse thermo-thickening property of the aqueous dispersion of hydrogel nanoparticles, and wherein above the Tg the first polymer network consists of crosslinked polymer chains inside each nanoparticle, and the second polymer network consists of a crosslinked system of the nanoparticles.

6. (Original) The aqueous dispersion of hydrogel nanoparticles of claim 5, wherein the inverse thermo-thickening property is a transformation from a low-viscous fluid to a gel when heated above the Tg.

7. (Original) The aqueous dispersion of hydrogel nanoparticles of claim 5, wherein the Tg is about 34°C.

8. (Cancelled).

9. (Cancelled).

10. (Cancelled).

11. (Previously Presented) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the IPN nanoparticles have a uniformed sized hydrodynamic radius.

12. (Previously Presented) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the IPN nanoparticles have an average hydrodynamic radius in the range from about 75 nm to about 200 nm.

13. (Previously Presented) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer and second polymer in the IPN nanoparticles have weight ratio of about 1:1.88.

14. (Original) The aqueous dispersion of hydrogel nanoparticles of claim 1, wherein the first polymer network and the second polymer network form a total polymer having a concentration range from about 1.25 wt% to about 5.25 wt% in distilled water.

15. (Previously Presented) A method of preparing an interpenetrating polymer network (“IPN”) of mono-disperse nanoparticles, comprising:

(a) providing a first mono-dispersed polymer prepared by mixing a first monomer, a surfactant, a first cross linking agent, and a first initiator at a first temperature wherein the first mono-dispersed polymer has a low critical solution temperature of between 28°C and 45°C, the first polymerization temperature is above the LCST of the first mono-dispersed polymer;

(b) adding to the first mono-dispersed polymer a second monomer, a second cross linking agent, a second initiator and an activator forming a nanoparticle solution, wherein the nanoparticle solution is an aqueous solution;

(c) mixing the nanoparticle solution for a period of time at a second temperature to form the IPN of mono-disperse nanoparticles; and

(d) isolating the IPN of mono-dispersed nanoparticles;
wherein the first monomer, the first cross linking agent, the second monomer, and the second cross linking agent are substantially free from dissolved oxygen gas and wherein the first mono-dispersed polymer forms a first polymer network which interpenetrates a second polymer network formed by the second polymer; and
wherein the second temperature is below the low critical solution temperature of the first monodispersed polymer.

16. (Original) The method of claim 15, further comprising (e) mixing the isolated IPN of mono-dispersed nanoparticles with a biologically active material at a third temperature.

17. (Original) The method of claim 16, wherein the biologically active material is a drug, a pro-drug, a protein, or a nucleic acid.

18. (Previously Presented) The method of claim 16, wherein the third temperature is below a gelation temperature (“Tg”) of the IPN of mono-disperse nanoparticles in an aqueous mixture, and wherein above the Tg the first polymer network consists of crosslinked polymer chains inside each nanoparticle, and the second polymer network consists of a crosslinked system of the nanoparticles.

19. (Original) The method of claim 18, wherein the Tg is about 33°C.

20. (Original) The method of claim 15, wherein the first mono-disperse polymer comprises poly(N-isopropylacrylamide) or hydroxypropylcellulose.

21. (Original) The method of claim 15, wherein the second monomer comprises poly(acrylic acid).

22. (Previously Presented) The method of claim 15, wherein the first mono-dispersed polymer nanoparticle comprises poly(N-isopropylacrylamide) and the second monomer comprises poly(acrylic acid).

23. (Original) The method of claim 15, wherein the first cross linking agent comprises N,N'-methylenebisacrylamide; the second cross linking agent comprises N,N'-methylenebisacrylamide; the first initiator comprises potassium persulfate; the second initiator comprises ammonium persulfate; the surfactant comprises sodium dodecyl sulfate (“SDS”) and the activator comprises TEMED.

24. (Original) The method of claim 15, wherein the IPN of mono-dispersed nanoparticles have an average hydrodynamic radius in the range from about 75 nm to about 200 nm.

25. (Original) The method of claim 15, wherein the period of time is less than 130 minutes.

26. (Previously Presented) The method of claim 25, wherein the period of time is about 120 minutes.

27. (Original) The method of claim 15, wherein the first temperature is about 70°C.

28. (Original) The method of claim 15, wherein the second temperature is about 21°C.

29. (Previously Presented) A method of preparing a nanocluster of cross-linked interpenetrating polymer networks (“IPN”) nanoparticles, comprising:

(a) providing a dispersion of IPN nanoparticles;

(b) adding a first cross linking agent and a second cross linking agent to the dispersion of IPN nanoparticles, forming an IPN cross linking solution; and

(c) heating the IPN cross linking solution to a first temperature for a period of time forming the nanocluster of cross-linked IPN nanoparticles;

wherein, the IPN nanoparticles have a uniformed size and comprise a first polymer network interpenetrating a second polymer network and is substantially free from a shell and core-shell polymer configuration a shell and core polymer configuration; the IPN nanoparticles can undergo a reversible gelation in response to a change in stimulus applied thereon; and

wherein the IPN nanoparticles exhibit a change in particle size of less than 30 nm when the IPN nanoparticles are heated from below a volume phase transition temperature to above a volume phase transition temperature at a concentration of 2.88×10^{-5} g/ml.

30. (Original) The method of claim 29, further comprising (d) mixing the nanocluster of cross-linked IPN's with a biologically active material at a second temperature.

31. (Previously Presented) The method of claim 30, wherein the biologically active material is a drug, a pro-drug, a protein, a nucleic acid, or a mixture thereof.

32. (Original) The method of claim 30, wherein the second temperature is below a gelation temperature ("Tg") of the nanocluster of cross-linked IPN nanoparticles in an aqueous dispersion.

33. (Original) The method of claim 32, wherein the Tg is about 33°C.

34. (Original) The method of claim 29, wherein the first polymer comprises poly(N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid).

35. (Original) The method of claim 29, wherein the first cross linking agent comprises 1-ethyl-3(3-dimethylaminopropyl) carbodiimide hydrochloride (“EDAC”); and the second cross linking agent comprises adipic acid dihydrazide.

36. (Original) The method of claim 29, wherein the nanocluster of cross-linked IPN’s an average hydrodynamic radius in the range from about 155 nm to about 250 nm.

37. (Original) The method of claim 36, wherein the nanocluster of cross-linked IPN’s have an average hydrodynamic radius in the range from about 225 nm to about 240 nm.

38. (Original) The method of claim 29, wherein the period of time is about 25 to about 45 minutes.

39. (Original) The method of claim 38, wherein the period of time is about 33 to about 37 minutes.

40. (Original) The method of claim 29, wherein the first temperature is about 44°C.

41. (Previously Presented) A nanocluster of cross-linked interpenetrating polymer network (“IPN”) nanoparticles, comprising: at least two IPN nanoparticles linked by a cross-linking group; wherein, the each IPN nanoparticle have a uniformed size and comprise a first polymer network interpenetrating a second polymer network and is substantially free from a shell-and core-shell polymer configuration.

42. (Original) The nanocluster of claim 41, further comprising a biologically active material.

43. (Previously Presented) The nanocluster of claim 42, wherein the biologically active material is a drug, a pro-drug, a protein, a nucleic acid, or a mixture thereof.

44. (Original) The nanocluster of claim 41, wherein the first polymer comprises poly(N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid).

Attorney Docket No.:
UNTD-0002 (122302.00085)

PATENT

45. (Original) The nanocluster of claim 41, wherein the cross linking group comprises adipic acid dihydrazide.

46. (Previously Presented) The nanocluster of claim 41, wherein the uniformed sized nanoparticles have an average hydrodynamic radius in the range from about 155 nm to about 1000 nm.

47. (Previously Presented) The nanocluster of claim 46, wherein the nanoparticles have an average hydrodynamic radius in the range from about 180 nm to about 250 nm.